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**APPLICATION OF ADVANCED NEURAL NETWORKS
IN HYPOGLYCEMIA DETECTION SYSTEM**

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(B.Eng. & M.Sc. & M.Eng.)

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Certificate of Authorship/Originality

I hereby declare that this thesis is my own work and effort and that it has not been submitted anywhere for any award. Any help that I have received in my research work and the preparation of the thesis itself has been acknowledged.

Signature

A handwritten signature in black ink, appearing to be 'PHYO PHYO SAN', written over a horizontal line.

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Contents

Acknowledgments	ii
Certificate of Authorship/Originality	iii
Contents	iv
Summary	xi
List of Figures	xvi
List of Tables	xx
Notation	xxii
Author's Publications	1
1 Introduction	4

1.1	Background	5
1.2	Motivation of Thesis	9
1.3	Objectives and Contributions	14
1.4	Structure of Thesis	18
2	Literature Review	21
2.1	Hypoglycemia	21
2.2	Physiological Disturbances in Hypoglycemia	25
2.2.1	Electrocardiography (ECG)	26
2.2.2	Sweating and Skin Impedances	33
2.2.3	Electroencephalogram (EEG)	34
2.3	Existing Technologies for Hypoglycemia Detection	36
2.3.1	Invasive Techniques	37
2.3.2	Non-invasive Techniques	39
2.4	Intelligent Detection of Hypoglycemia Using Physiological Parameters (Non-invasive Technique)	44
2.4.1	Fuzzy Reasoning Model	45

2.4.2	Fuzzy Neural Network	46
2.4.3	Neural Networks	47
2.4.4	Swarm-based fuzzy support vector machine (SVM)	49
2.4.5	GA-based Fuzzy Reasoning Model	50
2.5	The Proposed Methodologies for Hypoglycemia Detection	51
3	Optimized Variable Translation Wavelet Neural Network For Non-Invasive Hypoglycemia Detection	54
3.1	Introduction	54
3.2	Variable Translation Wavelet Neural Network (VTWNN)	56
3.2.1	Basis Wavelet Theory	58
3.2.2	Architecture of VTWNN	61
3.2.3	Design Parameters of VTWNN	66
3.3	Hybrid Particle Swam Optimization with Wavelet Mutation (HPSOWM)	67
3.3.1	Operation of wavelet mutation (WM)	74
3.3.2	Choosing parameters of HPSOWM	78
3.4	Case Study in Hypoglycemia Detection System	81

3.4.1	Analysis of electrocardiogram (ECG)	82
3.4.2	Data Set	85
3.4.3	Performance Evaluation	89
3.4.4	Fitness Function Formation	90
3.4.5	Experimental Results and Discussion	94
3.4.5.1	Statistical Correlation Analysis	98
3.4.5.2	Results Analysis	99
3.5	Conclusion	106
4	MR-based Combinational Neural Logic System and Its Application in Hypoglycemia Detection	108
4.1	Introduction	108
4.2	Design of MR-based Combinational Neural-Logic Network (NLN) . .	111
4.2.1	Combinational Neural-Logic Network (NLN)	112
4.2.1.1	Rule-Based AND Gate	113
4.2.1.2	Rule-Based OR Gate	114
4.2.1.3	Neural Network Operation	114

4.2.2	Design Example on Combinational Neural-Logic Network . . .	116
4.2.3	Multiple Regression Model	119
4.2.4	Design Parameters of MR-based Neural Logic Network	119
4.3	Training of MR-based NLN using HPSOWM	121
4.4	Case Study in Hypoglycemia Detection System	121
4.4.1	Experimental Results and Discussion	125
4.4.1.1	Results Analysis	128
4.5	Conclusion	132
5	Evolvable Rough-Block-Based Neural Network for Non-Invasive Hypoglycemia Detection	134
5.1	Introduction	134
5.2	Design and Architecture of Rough-Block-Based Neural Network . . .	139
5.2.1	Rough Set Preliminaries	140
5.2.2	Topology of Block Based Neural Network	142
5.2.2.1	Four Different Internal Configurations of BBNN . . .	144
5.2.3	Design Parameters of Rough-Block-Based Neural Network . .	147

5.3	Training of Rough-Block-Based Neural Network	148
5.4	Case Study in Hypoglycemia Detection System	149
5.4.1	Experimental Results and Discussion	152
5.4.1.1	Results Analysis	156
5.5	Conclusion	160
6	Summary and Discussion	162
6.1	Summary on the Characteristics of Network Topologies	163
6.2	Comparison Studies on Experimental Results	166
6.3	Summary	169
7	Conclusions and Further Research	172
7.1	Conclusions	172
7.2	Future Works	175
A	Artificial Neural Networks	177
A.1	Feed Forward Neural Network (FFNN)	179
A.2	Wavelet Neural Network (WNN)	181
A.3	Radial Basis Function Network (RBFNN)	183

A.4	Local Learning Algorithms	185
A.4.1	Hebbian Learning Rule	186
A.4.2	Back-propagation (BP) Learning Rule	187
A.5	Global Learning Algorithm	188
A.5.1	Genetic Algorithm (GA)	189
A.5.2	Particle Swarm Optimization (PSO)	191
A.5.3	Hybrid PSO with GA mutation (HGAPSO)	195
	Bibliography	197

Abstract

Hypoglycemia is the medical term for a state produced by lower levels of blood glucose. It represents a significant hazard in patients with Type 1 diabetes mellitus (T1DM) which is a chronic medical condition that occurs when the pancreas produces very little or no insulin. The imperfect insulin replacement places patients with T1DM at increased risk for frequent hypoglycemia. Deficient glucose counter-regulation in T1DM patients may even lead to severe hypoglycaemia even with modest insulin elevations. It is very dangerous and can even lead to neurological damage or death. Thus, continuous monitoring of hypoglycemic episodes is important in order to avoid major health complications.

Conventionally, the detection of hypoglycemia is performed by puncturing the fingertip of patients and estimate the blood glucose level (BGL) as well as the stage of hypoglycemia. However, the direct monitoring of BGL by extracting blood sample is inconvenient and uncomfortable, a more appealing preposition for preventing hypoglycemia is to monitor changes in relevant physiological parameters. Findings from

numerous studies indicate that sudden nocturnal death in type 1 diabetes is thought to be due to ECG QT prolongation with subsequent ventricular tachyarrhythmia in response to nocturnal hypoglycaemia. Though several parameters can be monitored, the most common physiological parameters to be effected from a hypoglycemic reaction are heart rate (HR) and corrected QT interval (QTc) of the ECG signal. Considering the real-time physiological parameters (HR and QTc) changes during hypoglycemia, a non-invasive monitoring of glycemic level is predicted for the hypoglycemia.

The topic of this thesis is covered by novel methodologies for the non-invasive hypoglycemia detection system by analyzing the behavioral changes of physiological parameters such as HR and QTc. These algorithms are comprised of three different classification techniques, i) variable translation wavelet neural network (VTWNN), ii) multiple regression-based combinational neural logic network (MR-NLN) and iii) rough-block-based neural network (R-BBNN). By taking the advantages of these proposed network structures, the performance in terms of sensitivity and specificity of non-invasive hypoglycemia monitoring system is improved.

The first proposed algorithm is VTWNN in which the wavelets are used as transfer functions in the hidden layer of the network. The network parameters, such as the translation parameters of the wavelets are variable depending on the network inputs. Due to the variable translation parameters, the proposed VTWNN has the ability

to model the inputoutput function with input-dependent network parameters. Effectively, it is an adaptive network capable of handling different input patterns and exhibits a better performance. With the adaptive nature, the network provides a better performance and increases the learning ability. For conventional wavelet neural network, a fixed set of weight is offered after the training process and fail to capture nonstationary nature of ECG signal. To overcome with this problem, VTWNN with multiscale wavelet function is firstly introduced in this thesis. With the variable translation parameter, the proposed VTWNN gives faster learning ability with better generalization.

The second algorithm, MR-NLN is systematically designed which is based on the characteristics of application. Its design is based on the binary logic gates (AND, OR and NOT) in which the truth table and K-map are constructed and it depends on the knowledge of application. Because the logic theory are used in the network design, the structure becomes systematic and simpler compared to other conventional neural networks (NNs) and enhance the training performance. Traditionally, the conventional NNs with the same structure are applied to handle different applications. The optimal performance may not always guaranteed due to different characteristics of applications. In real-world applications, the knowledge based-neural network that understands all the characteristics of practical applications are preferred for optimal performance. In conventional NNs, the redundant connections and weights of conventional neural networks make the number of network parameters unnecessarily large

and downgrades the training performance. But for neural logic network (NLN), the structure becomes simpler.

The third algorithm focuses on the hybridization technology using rough sets concepts and neural computing for decision and classification purposes. Based on the rough set properties, the input signal is partitioned to a predictable (certain) part and random (uncertain) part. In this way, the selected block-based neural network (BBNN) is designed to deal only with the boundary region which mainly consists of a random part of applied input signal and caused inaccurate modeling of data set. Due to the rough set properties and the adaptability of BBNN's flexible structures in dynamic environments, the classification performance is improved. Owing to different characteristics of neural network (NN) applications, a conventional neural network with a common structure may not be able to handle every applications. Based on the knowledge of application, BBNN is selected as a suitable classifier due to its modular characteristics and ability in evolving the size and structure of the network.

To obtain the optimal set of proposed network parameters, a global learning optimization algorithm called hybrid particle swarm optimization with wavelet mutation (HPSOWM) is introduced in this thesis. Compared to other stochastic optimization methods, the hybrid HPSOWM has comparable or even superior search performance for some hard optimization problems with faster and more stable convergence rates. During the training process, a fitness function which is characterized by the proposed network design parameters is optimized by reproducing a better fitness value.

The proposed systems is validated using clinical trial conducted at the Princess Margaret Hospital for Children in Perth, Western Australia, Australia. A total of 15 children with 529 data points (ages between 14.6 to 16.6 years) with Type 1 diabetes volunteered for the 10-hour overnight for natural occurrence of nocturnal hypoglycemia. Prior to the application of the algorithms, the correlation between the measured physiological parameters, HR and QTc and the actual BGL for each subject were analyzed. The feature extracted ECG parameters, HR and QTc significantly increased under hypoglycemic conditions ($BGL \leq 3.3mmol/l$) according to their respective p values, HR ($p < 0.06$) and QTc ($p < 0.001$). The observation on these changes within the physiological parameters have provided the groundwork for model classification algorithms.

List of Figures

2.1	Action for glucose and insulin in normal subject	22
2.2	Action for glucose and insulin in Type 1 diabetic patient	23
2.3	Hierarchy of Responses to Hypoglycemia [Wolpert2007]	25
2.4	Illustration of the normal electrocardiogram (ECG) signal	27
2.5	Typical QT measurement with on screen cursor placement from one subject during euglycemia: (a) showing a clearly defined T wave (b) showing prolonged repolarization [Marques1997]	28
2.6	QT measurement with tangent and non-tangent methods (a) a baseline ECG (b) a hypoglycemic ECG [Ireland2000]	30
2.7	Increased heart rate during hypoglycemia [Hilsted1984]	31
2.8	The effect of BGL on skin impedances [Ghevondian2001]	34
2.9	Electroencephalograms at different BGL from one patient [Pramming1988]	35

List of Figures

2.10	Overview of technologies for non-invasive blood glucose control: invasive, minimally invasive and non-invasive [Amaral2008]	37
2.11	A number of different electrochemical glucose meters [Clarke2012] . . .	38
2.12	GlucoWatch biographer: non-invasive glucose monitoring device [Vashist2012]	40
2.13	Block diagram for monitoring hypoglycemia in diabetic patients using fuzzy reasoning model [Ghevondian1997]	46
2.14	Proposed advanced neural networks based hypoglycemia detection system	52
3.1	Proposed architecture of the neural network [Ling2008c]	57
3.2	Diagram showing two sets of data in spatial domain [Ling2008c] . . .	58
3.3	Morlet wavelet [Ling2008]	60
3.4	Morlet wavelet dilated by parameter a [Ling2008]	61
3.5	Structure of Variable Translation Wavelet Neural Network	62
3.6	Maxican Hat Mother Wavelet	64
3.7	Nonlinear function with different values of parameter K	65
3.8	Effect of the shape parameter ζ_{wm} to a with respect to $\frac{t}{T}$	76
3.9	Effect of the parameter g to a with respect to $\frac{t}{T}$	78

3.10 Hybrid PSO based VTWNN hypoglycemia detection system	81
3.11 The normal ECG Signal	82
3.12 The lengthening of QTc interval under normal vs. hypoglycemic states	84
3.13 Actual blood glucose level profiles in 15 T1DM children	86
3.14 Fitness function with validation strategy	92
3.15 ROC curve analysis	101
4.1 The proposed MR-based combinational neural logic system	112
4.2 Internal Structure of Combinational Neural Logic System	112
4.3 K map: Design Example	117
4.4 The proposed combinational neural logic network for hypoglycemia monitoring system	121
4.5 K map: Hypoglycemia Detection	123
5.1 Proposed Rough-Block-Based neural network (R-BBNN)	140
5.2 Rough Set Approximation	141
5.3 Structure of Block-Based Neural Network	143
5.4 Internal configurations of block-based neural network	145

5.5	Hypoglycemia detection system using R-BBNN	149
5.6	(a) Positive lower boundary regions (b) Negative lower and boundary regions	151
5.7	Best Rough-block-based neural network (R-BBNN) structure	154
5.8	Best evolved block-based neural network structure (BBNN)	155
A.0.1	Model of artificial neuron	179
A.1.1	Structure of three layer feedforward neural network (FFNN)	180
A.2.1	Structure of wavelet neural network (WNN)	182
A.3.1	Structure of radial basic function neural network (RBFNN)	184

List of Tables

2.1	Studies of changes in QTc during euglycemic and hypoglycemic studies	32
2.2	Current non-invasive blood glucose/hypoglycemia monitors	43
2.3	ECG parameters and intelligent methods for hypoglycemia detection	44
3.1	The 15 patients and their associated hypoglycemia and non-hypoglycemia events	88
3.2	Changes in ECG parameters: HR and QTC under hypoglycemic con- ditions	98
3.3	Comparison studies: Area under ROC curve	100
3.4	Mean value of Training, Validation and Testing Results: Set specificity as $\eta_l = 40\%$	103
3.5	Best Testing Result for Hypoglycemia Detection with Different Ap- proaches as $\eta_l = 40\%$, 60% , and 80%	105

3.6	Best Testing Result for Hypoglycemia Detection as $\eta_l = 40\%$	106
4.1	Boundary Condition and Properties of The Neural Logic AND Gates	113
4.2	Boundary Condition and Properties of The Neural Logic OR Gates .	114
4.3	Truth Table: Design Example	117
4.4	Truth Table: Hypoglycemia Detection	123
4.5	Mean Value of Training, Validation and Testing Results as $\eta_l = 40\%$.	129
4.6	Best Testing Result for Hypoglycemia Detection as $\eta_l = 40\%$	130
4.7	Best Testing Result for Hypoglycemia Detection as $\eta_l = 50\%$	132
5.1	Mean Value of Training Validation and Testing Results as $\eta_l = 40\%$.	157
5.2	Best Testing Results as $\eta_l = 40\%$	159
6.1	Mean value of Training, Validation and Testing Results: Set maximum specificity, $\eta_{\max} = 40\%$	166
6.2	Best Testing Results: Set maximum specificity, $\eta_{\max} = 40\%$	168
6.3	Summary of the R-BBNN, MR-NLN and VTWNN	171

List of Symbols and Abbreviations

a	Dilation parameter of multi-wavelet
b	Translation parameter of multi-wavelet
n_{in}	Number of network inputs
n_h	Number of hidden nodes
n_{out}	Number of network outputs
$\psi_{a,b}(\cdot)$	Multi scaled wavelet function
$\psi(\cdot)$	Mother wavelet function
n_{para}	Total number of network parameters
$para_{max}^j$	Maximum value (Upper boundary) of particle element
$para_{min}^j$	Minimum value (Lower boundary) of particle element
v_{max}	Maximum velocity of particle
v_{min}	Minimum velocity of particle
$f(\cdot)$	Activation function
u_i	Input variables
v_{ij}	Weight between i th input and j th hidden nodes
w_{jl}	Weight between j th hidden and l th output nodes
b_j, b_l	Biases for hidden and output nodes
$logsig(\cdot)$	Logarithmic sigmoid transfer function
$tansig(\cdot)$	Hyperbolic tangent sigmoid transfer function
$pureline(\cdot)$	Liner transfer function
\vee	Maximum operator
\circ	Logic-AND operator
\bullet	Logic-OR operator
β	Regression parameters/coefficients
$\bar{I}(\cdot)$	Upper rough approximation region
$\underline{I}(\cdot)$	Lower rough approximation region
ζ_{wm}	Shape parameter of wavelet
μ_c	Probability of mutation

List of Symbols and Abbreviations

EEG	Electroencephalogram
ECG	Electrocardiographic
T1DM	Type 1 Diabetes Mellitus
QTc	Corrected QT Interval
HR	Heart Rate
CGMS	Continuous Glucose Monitoring System
VTWNN	Variable Translation Wavelet Neural Network
WNN	Wavelet Neural Network
FIS	Fuzzy Inference System
RBFINN	Radial Basis Function Network
FFNN	Flashforward Neural Network
WM	Wavelet Mutation
PSO	Particle Swarm Optimization
GA	Genetic Algorithm
BP	Back-propagation Learning
HPSOWM	Hybrid Particle Swarm Optimzation
HGAPSO	Hybrid PSO with GA mutation
ROC	Receiver Operating Characteristic
MR	Multiple Regression
NLN	Neural-Logic Network
BBNN	Block-Based Neural Network
BBNN	Block-Based Neural Network
R-BBNN	Rough-Block-Based Neural Network

Author's Publications

The contents of this thesis are based on the following papers that have been published, accepted, or submitted to peer-reviewed journals and conferences.

International Journal Papers:

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4. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen, "Evolvable Rough-Block-Based Neural Network and Its Biomedical Application", *IEEE Transactions on Systems, Man, and Cybernetics B*, Under Revision, July, 2012.
5. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen, "Application of Combinational Neural Logic System to Non-Invasive Hypoglycemic Monitor in Patients with T1DM", *IEEE Transactions on Systems, Man, and Cybernetics B*, Under Review, October, 2012.

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1. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen , "Combinational Neural Logic System and Its Industrial Application", *8th IEEE Conference on Industrial Electronics and Applications*, Melbourne, Australia, 19-21 June, pp. 947-952, 2013. (Finalist of IEEE ICIEA 2013 Best Paper Award)
2. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen , "Intelligent Detection of Hypoglycemic Episodes in Children with Type 1 Diabetes using Adaptive Neural-Fuzzy Inference System", *34th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, San Diego, California USA, August 28-September 1, pp. 6325-6328, 2012.
3. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen , "Optimized Variable Translation Wavelet Neural Network and Its Application in Hypoglycemia Detection

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4. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen , "Hybrid Particle Swarm Optimization Based Normalized Radial Basis Function Neural Network For Hypoglycemia Detection", *IEEE World Congress on Computational Intelligence*, Brisbane, Australia, 10-15 June, pp. 2718-2723, 2012.
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 6. Phyto Phyto San, Sai Ho Ling, and Hung T. Nguyen , "Non-invasive Detection of Hypoglycemic Episodes in Type1 Diabetes Using Intelligent Hybrid Rough Neural System", *35th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, Osaka, Japan, July 3-7, Submitted, 2013.

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